Title: **Multi-scale mechanics of the tendon-to-bone attachment**

Authors: Stavros Thomopoulos, Victor Birman, Markus J. Buehler, Ioannis Chasiotis, Iden Kurtaliaj, Mikhail Golman, Roger A. Rowe, Kenneth M. Pryse, Brittany Marshall, Ethan D. Hoppe, Fei Li, Donghwan Eric Yoon, Jiahao Wei, Steve Linderman, Pedro Ponte-Castañeda, John C. Boyle, Alix C. Deymier-Black, Zhao Qin, Fatemeh Sadaat, Guy M. Genin

Presenter: Guy M. Genin

Surgical repair of rotator cuff and anterior cruciate ligament tears requires re-attachment of tendon to bone. Outcomes after repair are poor, leading to significant pain, disability, and repeated surgery. The reason for high failure rates after repair is the difficulty of attaching two materials, tendon and bone, that have a large mismatch in their mechanical properties. The health attachment tissue between tendon and bone meets this mechanical challenge through a number of mechanisms across multiple length scales that create a strong and tough attachment. Unfortunately, the healing attachment does not regenerate this transitional tissue. Our aim is therefore to develop multiscale models to better understand this natural material system, with the hope of defining the design criteria for a tissue engineered construct.

Experimentally, we are testing hypotheses that the interface at the tendon-to-bone insertion presents toughening mechanisms through: i) nanometer- to micrometer-scale spatial gradients in mineral content and collagen fiber organization, ii) a micrometer scale compliant region, iii) a micrometer scale interdigitation geometry, and iv) a millimeter scale footprint area with a splayed insertion morphology. Through multiscale models, we are testing hypotheses that: i) gradients in collagen orientation and patterns of mineral accumulation explain the compliant region, ii) percolation of mineral on collagen fibers determines the nature of stress transfer between tendon and bone, iii) a compliant region and interdigitation geometry minimizes stress concentrations and toughens the attachment between tendon and bone, and iv) a large attachment footprint and splayed insertion geometry improve load transfer by reducing stresses at the interface.

Ongoing efforts are combining models of collagen-mineral interactions at the nanoscale with data for collagen orientation and mineral content at the microscale to produce a multiscale assessment of tendon-to-bone insertion mechanics. A central theme that is emerging is a key role of stochastic processes in controlling the resilience of the otherwise highly ordered tissue interface between tendon and bone. Using these results, we have begun to develop guidelines for tissue engineering efforts and have begun translating our work to identify metrics of tendon-to-bone tissue health noninvasively.